Subject: RE: statement from UC San Diego
From: "Carr, Jacqueline" <jcarr@ucsd.edu>
Date: 4/15/19, 4:38 PM
To: Brad Racino <bradracino@inewsource.org>
CC: "Lafee, Scott" <slafee@ucsd.edu>

Hi Brad- I am sending this in sections. Here you go:

1) **Suspension**: I understand that Dr. Zhang is suspended indefinitely from serving on all UCSD IRB protocols, though he is allowed to be a PI on a grant, which has different responsibilities – none of which relate to overseeing a human research project. UCSD communicated extensively with the FDA about Zhang's restrictions, and CIRM was also made aware (according to Dr. Zhang). However, **was the NIH, ORI, OHRP, CMB or San Diego VA made aware of these restrictions or the audit's findings.**

   These entities were not made aware of these restrictions as the reports were made in response to specific studies.

2. **Reviewing past work**: The AMAS report did include studies that were no longer active but it did not include other active studies at the time, such as "Limbal Stem Cell Fate and Corneal Specific Enhancers" and the previously mentioned "Molecular Mechanism and Therapy for Ocular Melanoma" study. Since the FDA Warning Letter that prompted the AMAS report included research violations that could have happened in any study – human trial or not – **why did the AMAS report focus only on human subjects research**?

   The AMAS report was initiated due to concerns regarding human subjects research in response to a request by the IRB, which does not have oversight for non-human subjects research.

3. **IRB** and **Research Compliance**: Your email said "The IRB Office does not have an audit function." But section 5.1 of the UCSD HRPP IRB SOPP states:
   "*When the IRB opts to assess the conduct of the study or the consent process as part of providing adequate oversight, an audit is conducted by the IRB Chair, a member of the IRB, a member of another IRB or an unaffiliated party. An audit may be study-oriented (focused on a specific study) or investigator-oriented (focused on all the studies of a particular investigator). An audit may be also be classified as routine (part of the normal oversight process) or 'for cause'*."

   a. Should I be interpreting that to mean the IRB *could* have an audit function but does not, and the actual SOP is to have the Research Compliance officer do the audit?
   b. Your email said "Research Compliance performs regular audits, reviews documentation such as consent and case report forms, and reviews overall study compliance." In the Zhang studies that had violations related to documentation, consent, and compliance, **what happened with that Research Compliance officer**? Did he/she miss things? Did the reviews never happen? The Genentech study – inspected by the FDA in 2016 – had been

going on since July 2011. What happened?

The IRB could audit. Research Compliance can also conduct audits. In this case, AMAS conducted the audit in question at the request of the IRB. Zhang's research had undergone multiple audits since 2012. The audits prompted a series of actions that culminated in the AMAS report and subsequent indefinite suspension.

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From: Brad Racino [mailto:bradracino@inewsource.org]
Sent: Thursday, April 11, 2019 3:02 PM
To: Lafee, Scott <slafee@ucsd.edu>
Cc: Carr, Jacqueline <jcarr@ucsd.edu>
Subject: Re: statement from UC San Diego

Thanks.

Lafee, Scott

April 11, 2019 at 2:56 PM

Brad:
Jackie's out of office so I'm stepping back in. I've forwarded your questions for clarification. Back as soon as we have a reply.
Scott

From: Brad Racino [mailto:bradracino@inewsource.org]
Sent: Thursday, April 11, 2019 2:30 PM
To: Carr, Jacqueline <jcarr@ucsd.edu>
Cc: Lafee, Scott <slafee@ucsd.edu>
Subject: Re: statement from UC San Diego

Thank you Jackie, I appreciate the fast responses. Because this is a delicate

topic, I want to make sure I'm reading your responses as accurately as possible and leaving no room for error on my part. Therefore I have some clarification questions.

1. **Suspension**: I understand that Dr. Zhang is suspended indefinitely from serving on all UCSD IRB protocols, though he is allowed to be a PI on a grant, which has different responsibilities – none of which relate to overseeing a human research project. UCSD communicated extensively with the FDA about Zhang's restrictions, and CIRM was also made aware (according to Dr. Zhang). However, **was the NIH, ORI, OHRP, CMB or San Diego VA made aware of these restrictions or the audit's findings?**

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Sorry if I'm overloading you, but I really don't want to misinterpret anything.

-Brad

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Brad Racino

April 11, 2019 at 2:29 PM

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Sorry if I'm overloading you, but I really don't want to misinterpret anything.

-Brad

Carr, Jacqueline

April 11, 2019 at 7:43 AM

Hi Brad- Here you go:

1. As answered, Dr. Zhang's suspension as a PI on protocols is ongoing. The findings were limited to human subjects research.
2. Extensive communications were conducted with FDA, including a summary of the restrictions on Dr. Zhang's human subjects research. Dr. Zhang informed the IRB that he made CIRM aware of the protocol violations for CIRM sponsored research and he indicated that CIRM provided a response to his notification.
3. The findings from the AMAS audit were limited to UCSD research.
4. The AMAS report included studies that were no longer active.

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From: Brad Racino [bradracino@inewsource.org]
Sent: Wednesday, April 10, 2019 11:40 AM
To: Carr, Jacqueline
Cc: Lafee, Scott
Subject: Re: statement from UC San Diego

Thank you Jackie. I'm hoping you can answer some follow-up questions as soon as possible.

1. How long was Dr. Zhang's suspension? Or is it still ongoing? And why only clinical trials opposed to any research involving human subjects?
2. Did UCSD alert any oversight agencies, such as the NIH, FDA, OHRP, ORI, or California Medical Board to its audit findings?
3. In the same vein, did UCSD alert any institutions where Zhang conducts research, including the San Diego VA?
4. The audit examined Zhang's current research. Did UCSD look at any other previous research he had done? If not, please explain the reasoning, considering its finding violations in 100 percent of the studies that involved enrolled human subjects.

I appreciate the help.

-Brad

Brad Racino

April 10, 2019 at 11:40 AM

Thank you Jackie. I'm hoping you can answer some follow-up questions as soon as possible.

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I appreciate the help.

-Brad

Carr, Jacqueline

April 10, 2019 at 10:57 AM

Hi Brad- Thank you for your patience in waiting for a response. Here is the statement from UC San Diego related to Dr. Kang Zhang:

MEDIA STATEMENT
As a result of the 2017 FDA warning letter and subsequent UCSD

Ophthalmology Human Subjects Research Compliance report you referenced, UC San Diego implemented a comprehensive management action plan to address these issues, including document corrections, retraining key personnel, requiring a secondary screening process, and suspending Dr. Kang Zhang from serving as principal investigator (PI) on any protocols.

Best, Jackie

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Good afternoon Jackie,

In the course of researching the human research study done at the San Diego VA, we came across a UC audit and FDA warning letter specific to Dr. Kang Zhang, who is the Chief of Ophthalmic Genetics and a Professor of Ophthalmology at UCSD.

The audit and warning letter found a number of problems with several of Zhang's studies. We have passed the findings along to several experts for their review, and so far all have said the major findings are troubling and appear to show a pattern.

We would like to interview Dr. Zhang and/or Robert Weinreb – the chair of the Shiley Eye Institute where Dr. Zhang works – about the audit and letter, any corrective actions taken and steps to ensure future compliance.

Please let me know if you can help arrange that interview, and/or provide any additional context, findings, reviews or relevant documents related to Dr. Zhang's research.

Thank you for your help.

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